ORAL CONTRIBUTIONS

829 Newer Therapies for Stable Coronary Artery Disease

Monday, March 31, 2003, 4:00 p.m.-5:30 p.m.
McCormick Place, Room S102

4:00 p.m.

829-1 Combined Intense Lifestyle and Pharmacologic Lipid Treatment Further Reduce Coronary Events and Myocardial Perfusion Abnormalities Compared to Usual Care Cholesterol Lowering Drugs in Coronary Artery Disease

Stefano Sdringola, Keiichi Nakagawa, Yuko Nakagawa, Wamique S. Yusuf, Fernando Boccalandro, Nizar Mullani, Mary Haynie, Mary Jane Hess, K. Lance Gould, The Weatherhead P.E.T. Center, University of Texas Medical School Houston, Houston, TX

Background: Lifestyle and lipid drugs separately benefit Coronary Artery Disease (CAD). Objective: Determine if combined intense lifestyle and pharmacologic lipid treatment reduce myocardial perfusion abnormalities and coronary events versus usual care cholesterol lowering drugs and whether perfusion changes predict outcomes.
Methods: 409 patients with CAD and myocardial perfusion imaging by dipyridamole PET at baseline and after 2.6 years had quantitative size/severity of perfusion defects measured objectively by automated software with complete follow-up on all patients for 5 more years for revascularization, non fatal myocardial infarction or cardiac death. Patients were categorized blindly by prospective predefined criteria as Poor treatment without diet or lipid drugs, or smoking; Moderate treatment on AHA diet and lipid lowering drugs or on strict low fat diet (<10% of calories) without lipid drugs; Maximal treatment with diet <10% of calories as fat, regular exercise and lipid active drugs dosed to target goals of LDL 1.2mmol/L (45 mg/dl) and triglycerides < 1.1mmol/L (100 mg/dl).
Results: Over 5 years, coronary events occurred in 6.6%, 20.3% and 30.6% of patients on Maximal, Moderate and Poor treatment respectively (p= 0.001). Size/severity of perfusion abnormalities significantly decreased for Maximal and increased for Moderate and Poor treatment (p=0.003 and 0.0001). Combined intense life style change plus lipid active drugs and severity/change of perfusion abnormalities independently predicted cardiac events.
Conclusions: Intense life style and pharmacologic lipid treatment reduce size/severity of myocardial perfusion abnormalities and cardiac events compared to usual-care cholesterol lowering drugs. Perfusion changes parallel treatment intensity and predict clinical outcomes.

4:15 p.m.

829-2 Clopidogrel Inhibits Exercise-Induced Ischemia and Platelet Activation in Stable Coronary Artery Disease

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Background:Exercise stimulates coagulation, and thrombocytosis and may trigger the clinical presentation of acute coronary syndrome. Aspirin provides little protection against exercise induced platelet activation in normal subjects however the effects in coronary artery disease (CAD) are controversial. Hypothesis: Clopidogrel inhibits platelet activation and provides additional benefits over aspirin in the prevention of exercise induced haemostatic changes Methods: 21 patients with CAD awaiting Percutaneous Coronary Intervention performed two Bruce protocol exercise tests while receiving 1)Aspirin 75mg only and 2)aspirin 75mg+clopidogrel 75mg (300mg loading dose+7 days of 75mg). Blood sampling was performed pre, immediately post and 30 minutes post exercise. Platelet activation was assessed using flow cytometry. CD62(p-selectin) and antifibrinogen antibody were used to assess platelet activation at rest and in response to ADP and Epinephrine. All patients performed an exercise test prior to the study for familiarisation and samples were blinded for analysis. Results: Data are expressed as mean (SD) or median (Interquartile range) when non-parametric test was used. Exercise time increased (488(112)seconds to 587(129)seconds p=0.004) and exercise induced ST depression was reduced (-1.8mm(0.9), -1.0(0.6) p=0.04) on aspirin/clopidogrel compared to aspirin alone. Anti-fibrinogen antibody binding was reduced at rest(11.2.%(3.4,22.9), 3.8%(1.1,5.8), p=0.07) as was serum fibrinogen (2.98(2.5,3.3), 2.53(2.24,2.9) p=0.06)with the addition of clopidogrel. Clopidogrel abolished the platelet response to ADP at all stages of exercise, however most markedly immediately post exercise. (%CD62 42.9(38.2,61.4), 20.5 (18.4,32.9) p=0.008, %Anti-fibrinogen 78.0 (54.2, 91.8.) to 37.2(20.6, 52.2) p=0.009). Conclusion: Clopidogrel improves functional capacity and exercise induced ST changes as well as reducing platelet activation. This suggests that even in stable angina, superimposed thrombus may be an important factor in precipitating ischaemia, requiring more aggressive anti-platelet therapy than aspirin alone.

4:30 p.m.

829-3 Enhanced External Counterpulsation Improves Endothelial Function in Patients With Coronary Artery Disease

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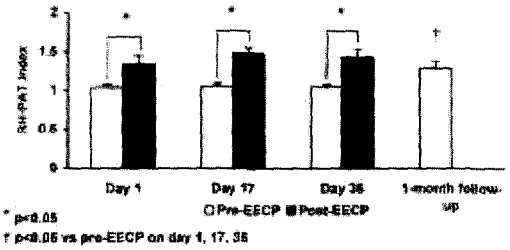
Background: Enhanced external counterpulsation (EECP) is a non-invasive procedure that reduces symptoms and improves exercise tolerance in patients with coronary artery disease (CAD). However, the mechanisms by which this technique exerts its benefit are unclear. This study was designed to investigate the effect of EECP on endothelial function, as measured by Reactive Hyperemia Peripheral Arterial Tonometry (RH-PAT), a novel, non-invasive technique to assess peripheral microvascular endothelial function in the finger. Methods: 23 patients with symptomatic CAD despite optimal medical therapy (mean age 66 years, mean CCS class 3.3) underwent a 35-hour EECP course over 7 weeks. RH-PAT measurements were performed before and after the first, a mid-course, and the last EECP session. In addition, RH-PAT response and functional status were assessed one month after EECP treatment. RH-PAT index, a measure of reactive hyperemia, was calculated as the ratio of the digital pulse volume during the first minute of reactive hyperemia divided by that at rest. Results: Average CCS class was significantly lower immediately and one month after the course of EECP (3.3 vs. 2.4 vs. 2.3, p<0.05). As shown in the figure, EECP increased RH-PAT index immediately and at 1 month follow-up. Conclusion: EECP is associated with improvement in endothelial function which



may serve as a potential mechanism contributing to the symptomatic benefit of EECP in patients with CAD.

4:45 p.m.

829-4 Preserved Benefit of Enhanced External Counterpulsation in End Stage Ischemic Heart Disease

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Background: Enhanced External Counterpulsation (EECP) is a non-invasive device effective for angina in coronary (CAD) patients (pts). EECP is used in pts refractory to medicine who are poor candidates for angioplasty (PCI) or bypass (CABG). Whether prior PCI or CABG, or when EECP is begun, effects immediate benefit or durability of effect is unknown.
Methods: The IEPR is a prospective, sequential registry characterizing and following angina pts treated with EECP. Pts with prior PCI or CABG are included. The demographics, immediate and sustained (1 year) outcomes with prior PCI alone (PCI group) were compared to those with prior CABG (CABG group).
Results: There were 252 PCI pts and 947 CABG (69.2% prior PCI) pts. The CABG pts were older (66.3 ± 10.3 vs 63.7 ± 11.6 years; p<0.005), more males (76.8 vs 68.3%; p<0.005), longer duration of CAD (12.5 ± 7.9 vs 6.0 ± 6.0 years; p<0.001), more infarcts (72.2 vs 62.7%; p<0.005), more heart failure (33.7 vs 26.7%; p<0.01), more multivessel CAD (90.9 vs 47.3%; p<0.001), and a lower ejection fraction (45.1 ± 13.8 vs 49.0 ± 14.8; p<0.001). Only 9.9% of the CABG group were revascularization candidates versus 20.4% of the PCI group (p<0.001). Baseline CCS angina class was worse in the CABG group (p<0.01). PCI vs CABG group pts received EECP a mean of 32.5 ± 10.3 vs 33.1 ± 10.3 hrs; incomplete rate was higher in the PCI group, 11.9 vs 7.0 % (p<0.01). There were no differences in immediate major (death, unstable angina, MI, CHF, CABG or PCI) or minor (musculoskeletal or skin) events. Angina decreased ≥1 angina class in 69.9 % of PCI and 71.4% of CABG pts; p=NS. At one year 74.4% of PCI and 74.2% of CABG pts had no angina or were in CCS class I/II; 69.9% of PCI and 70.0% of CABG pts maintained initial reduction in angina. No excess major events or hospitalizations were noted at 1 year in the CABG group.
Conclusion: Similar treatment success and durability of benefit, with similar event rates and mortality, are seen after treatment with EECP in pts previously treated with PCI or CABG. This benefit is demonstrated despite CABG pts being older, with more extensive CAD and prior infarcts, more heart failure, and more severe angina. EECP retains its effectiveness, used as a treatment of last resort for angina.